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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/085,820	05/28/1998	HAI U. WANG	CTCH-P02-006	7434
28120	7590	03/22/2004	EXAMINER	
ROPES & GRAY LLP ONE INTERNATIONAL PLACE BOSTON, MA 02110-2624			ANDRES, JANET L	
			ART UNIT	PAPER NUMBER
			1646	

DATE MAILED: 03/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<p align="center">Office Action Summary</p>	Application No. 09/085,820	Applicant(s) WANG ET AL.	
	Examiner Janet L. Andres	Art Unit 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 November 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 153-240 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 235-240 is/are allowed.
- 6) ☒ Claim(s) 153-178, 182-185, 192-222 and 227-234 is/are rejected.
- 7) ☒ Claim(s) 179-181, 186-191 and 223-226 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>24 November 2003</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 24 November 2003 has been entered. Claims 153-240 are pending and under examination in this office action.

Claim Rejections Withdrawn

2. The rejection of claims 154-194 and 232-240 as lacking enablement because the function of soluble receptors, ligands, and antibodies is unpredictable is withdrawn in response to Applicant's arguments.

Claim Rejections - 35 USC § 112

3. Claims 153-178, 182-185, 192-222, and 227-234 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of enhancing or inhibiting angiogenesis using ephB4 or ephrinB2 peptides or antibodies against ephB4 or ephrinB2, does not reasonably provide enablement for methods requiring other ephs or ephrins, methods of alteration that are not enhancement or inhibition, or methods using antagonists or inhibitors. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the the invention commensurate in scope with these claims.

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Claims 153-177, 195-212, and 232-234 encompass methods using ephrins and ephs other than ephrinB2 and ephB4. These claims require that the ephrins and ephs used be selectively expressed on arterial or venous cells. However, while other ephrins and ephs, such as ephrin A1, ephrin B1, eph A2, and eph B1 have been identified as being involved in angiogenesis, they do not appear to be selectively expressed. Adams, cited previously by Applicant in the response of 25 March 2002, teaches involvement of other ephs and ephrins in angiogenesis but not the required selective expression. Since neither the art nor Applicant teaches selective expression of any other ephs or ephrins, it is not predictable that such selectively expressed molecules exist. Thus, while the techniques for identifying other molecules that could be used as claimed are straightforward, neither the art nor Applicant provides an expectation of success. The provision of art-recognized procedure is not adequate guidance as to what other molecules are selectively expressed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. What is provided is thus the idea for an invention, and the invitation to experiment to implement this invention, not the invention itself.

Claims 153, 174, and 232 encompass "alterations" in angiogenesis or blood vessel development. They thus encompass more than activation or inhibition of eph or ephrin-mediated processes. Applicant has not described such alterations or the agents capable of causing them; thus one of skill in the art could not practice the methods as broadly claimed.

Claims 153-157, 161-164, 174-178, 182-185, 192-205, 213-222, and 227-231 encompass agonists and antagonists that are not portions of ephB4, ephrinB2, or antibodies against these two molecules. Applicant has not described the characteristics of all such molecules, which include such agents as small organic molecules that are unrelated in structure to the ephs and ephrins that

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have been described. Since the genus of all agonists and antagonists of ephs and ephrins has not been described, the skilled artisan could not make and use them as claimed.

4. Claims 153-178, 182-185, 192-222, and 227-234 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

As stated above, claims 153-177, 195-212, and 232-234 encompass methods using ephrins and ephs other than ephrinB2 and ephB4. These molecules must be artery or vein specific. However, Applicant has not described the characteristics of such artery or vein specific molecules. While the characteristics of ephs and ephrins are known, the characteristic features of ephs and ephrins that are expressed selectively in arteries or veins are not described. Since the relevant features that result in or are characteristic of selective expression are not set forth, the artisan would not conclude that Applicant was in possession of this genus of molecules.

Also as stated above, claims 153, 174, and 232 encompass "alterations" in angiogenesis or blood vessel development. They thus require agents that do something other than enhance or inhibit angiogenesis. Applicant has not described any characteristics of agents capable of causing such alterations and the skilled artisan would not conclude that Applicant was in possession of such agents.

Also as stated above, claims 153-157, 161-164, 174-178, 182-185, 192-205, 213-222, and 227-231 encompass agonists and antagonists that are not portions of ephB4, ephrinB2, or antibodies against these two molecules. Applicant has not described the characteristics of all

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such molecules, which include such agents as small organic molecules that are unrelated in structure to the ephs and ephrins that have been described, or to antibodies against them. Thus the artisan would not conclude that Applicant was in possession of the genus of all agonists and antagonists of ephs and ephrins.

Allowable Subject Matter

5. Claims 179-181, 186-191, and 223-226 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

CLAIMS 153-178, 182-185, 192-222, AND 227-234 ARE REJECTED. CLAIMS 179-181, 186-191, AND 223-226 ARE OBJECTED TO. CLAIMS 235-240 ARE ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Andres whose telephone number is 571-272-0867. The examiner can normally be reached on Monday-Thursday and every other Friday, 8:00-5:30.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 571-272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Janet L. Andres, Ph.D.

18 March 2003


JANET ANDRES
PATENT EXAMINER